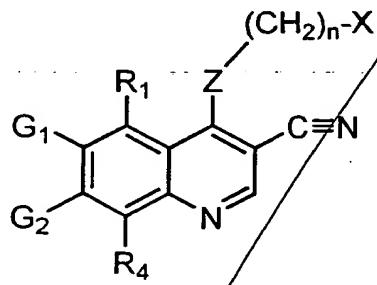


- 119 -

**WHAT IS CLAIMED IS:**

1. A compound of Formula 1 having the structure:



wherein:

X is cycloalkyl of 3 to 7 carbon atoms, which may be optionally substituted with one or more alkyl of 1 to 6 carbon atom groups; or is a pyridinyl, pyrimidinyl, or phenyl ring wherein the pyridinyl, pyrimidinyl, or phenyl ring may be optionally mono-, di-, or tri-substituted with a substituent selected from the group consisting of halogen, alkyl of 1-6 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl of 2-6 carbon atoms, azido, hydroxyalkyl of 1-6 carbon atoms, halomethyl, alkoxymethyl of 2-7 carbon atoms, alkanoyloxymethyl of 2-7 carbon atoms, alkoxy of 1-6 carbon atoms, alkylthio of 1-6 carbon atoms, hydroxy, trifluoromethyl, cyano, nitro, carboxy, carboalkoxy of 2-7 carbon atoms, carboalkyl of 2-7 carbon atoms, phenoxy, phenyl, thiophenoxy, benzoyl, benzyl, amino, alkylamino of 1-6 carbon atoms, dialkylamino of 2 to 12 carbon atoms, phenylamino, benzylamino, alkanoylamino of 1-6 carbon atoms, alkenoylamino of 3-8 carbon atoms, alkynoylamino of 3-8 carbon atoms, carboxyalkyl of 2-7 carbon atoms, carboalkoxyalkyl of 3-8 carbon atoms, aminoalkyl of 1-5 carbon atoms, N-alkylaminoalkyl of 2-9 carbon atoms, N,N-dialkylaminoalkyl of 3-10 carbon atoms, N-alkylaminoalkoxy of 2-9 carbon atoms, N,N-dialkylaminoalkoxy of 3-10 carbon atoms, mercapto, and benzoylamino;

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120

- 120 -

Z is -NH-, -O-, -S-, or -NR- ;

R is alkyl of 1-6 carbon atoms, or carboalkyl of 2-7 carbon atoms;

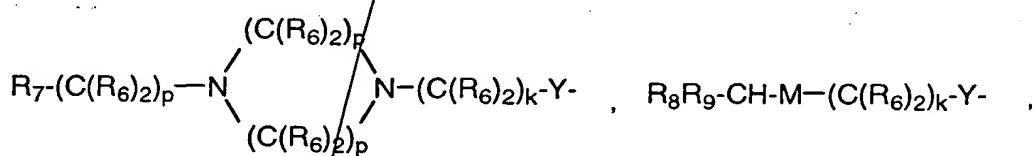
G<sub>1</sub>, G<sub>2</sub>, R<sub>1</sub>, and R<sub>4</sub> are each, independently, hydrogen, halogen, alkyl of 1-6 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl of 2-6 carbon atoms, alkenyloxy

5 of 2-6 carbon atoms, alkynyoxy of 2-6 carbon atoms, hydroxymethyl, halomethyl, alkanoyloxy of 1-6 carbon atoms, alkenoyloxy of 3-8 carbon atoms, alkynoyloxy of 3-8 carbon atoms, alkanoyloxymethyl of 2-7 carbon atoms, alkenoyloxymethyl of 4-9 carbon atoms, alkynoyloxymethyl of 4-9 carbon atoms, alkoxy of 1-6 carbon atoms,

10 alkylthio of 1-6 carbon atoms, alkylsulphinyl of 1-6 carbon atoms, alkylsulphonyl of 1-6 carbon atoms, alkylsulfonamido of 1-6 carbon atoms, alkenylsulfonamido of 2-6 carbon atoms, alkynylsulfonamido of 2-6 carbon atoms, hydroxy, trifluoromethyl, trifluoromethoxy, cyano, nitro, carboxy, carboalkoxy of 2-7 carbon atoms, carboalkyl of 2-7 carbon atoms, phenoxy,

15 phenyl, thiophenoxy, benzyl, amino, hydroxyamino, alkoxyamino of 1-4 carbon atoms, alkylamino of 1-6 carbon atoms, dialkylamino of 2 to 12 carbon atoms, N-alkylcarbamoyl, N,N-dialkylcarbamoyl, N-alkyl-N-alkenylamino of 4 to 12 carbon atoms, N,N-dialkenylamino of 6-12 carbon atoms, phenylamino, benzylamino,

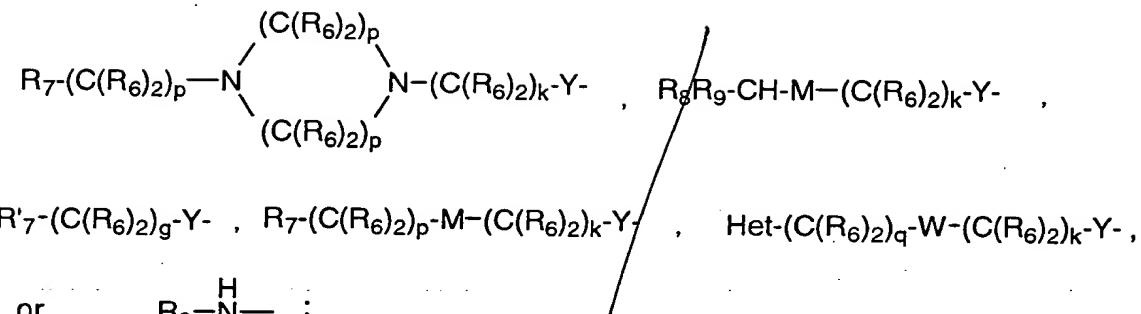
20



$\text{R}_7-(\text{C}(\text{R}_6)_2)_g-\text{Y-}$ ,  $\text{R}_7-(\text{C}(\text{R}_6)_2)_p-\text{M-}(\text{C}(\text{R}_6)_2)_k-\text{Y-}$ , or  $\text{Het-(C(R}_6)_2)_q-\text{W-(C(R}_6)_2)_k-\text{Y-}$

with the proviso that either G<sub>1</sub> or G<sub>2</sub> or both G<sub>1</sub> and G<sub>2</sub> must be a radical selected from the group

- 121 -



Y is a divalent radical selected from the group consisting of

5 
$$-(\text{CH}_2)_a- , -\text{O}- , \text{ and } -\overset{\text{H}}{\underset{|}{\text{N}}}-R_6- ;$$

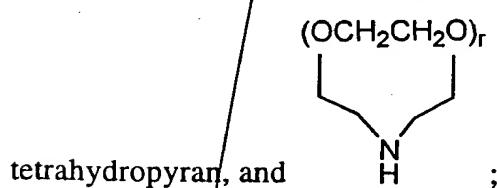
R<sub>7</sub> is  $-\text{NR}_6\text{R}_6$ ,  $-\text{J}$ ,  $-\text{OR}_6$ ,  $-\text{N}(\text{R}_6)_3$ , or  $-\text{NR}_6(\text{OR}_6)$ ;

10 R'<sub>7</sub> is  $-\text{NR}_6(\text{OR}_6)$ ,  $-\text{N}(\text{R}_6)_3^+$ , alkenoxy of 1-6 carbon atoms, alkynoxy of 1-6 carbon atoms, N-alkyl-N-alkenylamino of 4 to 12 carbon atoms, N,N-dialkenylamino of 6-12 carbon atoms, N-alkyl-N-alkynylamino of 4 to 12 carbon atoms, N-alkenyl-N-alkynylamino of 4 to 12 carbon atoms, or N,N-dialkynylamino of 6-12 carbon atoms with the proviso that the alkenyl or alkynyl moiety is bound to a nitrogen or oxygen atom through a saturated carbon atom;

M is  $>\text{NR}_6$ ,  $-\text{O}-$ ,  $>\text{N-(C(R}_6)_2)_p\text{NR}_6\text{R}_6$ , or  $>\text{N-(C(R}_6)_2)_p\text{OR}_6$ ;

15 W is  $>\text{NR}_6$ ,  $-\text{O}-$  or is a bond;

Het is a heterocycle selected from the group consisting of morpholine, thiomorpholine, thiomorpholine S-oxide, thiomorpholine S,S-dioxide, piperidine, pyrrolidine, aziridine, pyridine, imidazole, 1,2,3-triazole, 1,2,4-triazole, thiazole, thiazolidine, tetrazole, piperazine, furan, thiophene, 20 tetrahydrothiophene, tetrahydrofuran, dioxane, 1,3-dioxolane, ,



- 122 -

wherein the heterocycle is optionally mono- or di-substituted on carbon or nitrogen with R<sub>6</sub>, optionally mono- or di-substituted on carbon with hydroxy, -N(R<sub>6</sub>)<sub>2</sub>, or -OR<sub>6</sub>, optionally mono or di-substituted on carbon with the mono-valent radicals -(C(R<sub>6</sub>)<sub>2</sub>)<sub>s</sub>OR<sub>6</sub> or -(C(R<sub>6</sub>)<sub>2</sub>)<sub>s</sub>N(R<sub>6</sub>)<sub>2</sub>, or optionally mono or di-substituted on a saturated carbon with divalent radicals -O- or -O(C(R<sub>6</sub>)<sub>2</sub>)<sub>s</sub>O-;

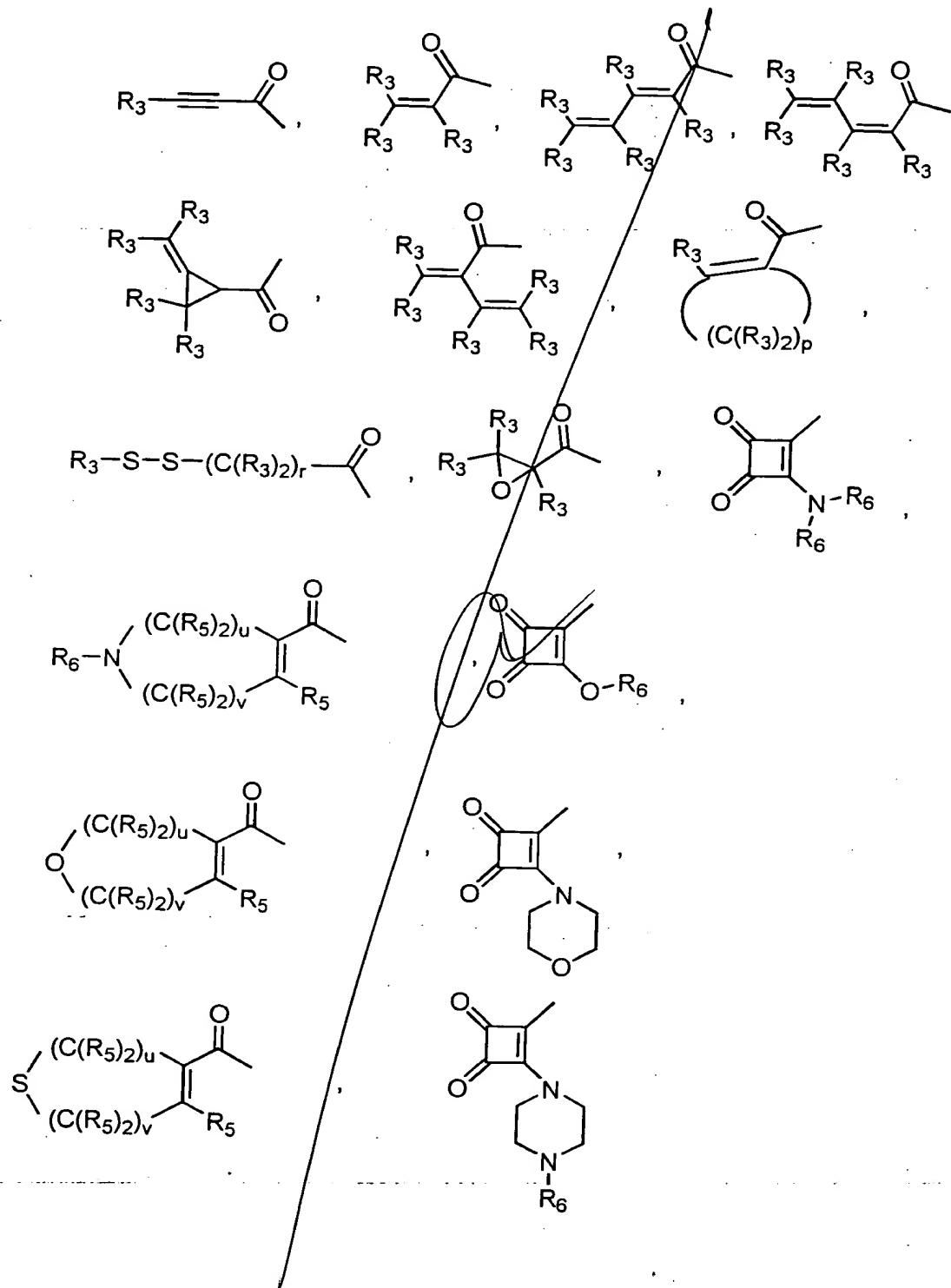
R<sub>6</sub> is hydrogen, alkyl of 1-6 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl of 2-6 carbon atoms, cycloalkyl of 1-6 carbon atoms, carboalkyl of 2-7 carbon atoms, carboxyalkyl (2-7 carbon atoms), phenyl, or phenyl optionally substituted with one or more halogen, alkoxy of 1-6 carbon atoms, trifluoromethyl, amino, alkylamino of 1-3 carbon atoms, dialkylamino of 2-6 carbon atoms, nitro, cyano, azido, halomethyl, alkoxymethyl of 2-7 carbon atoms, alkanoyloxymethyl of 2-7 carbon atoms, alkylthio of 1-6 carbon atoms, hydroxy, carboxyl, carboalkoxy of 2-7 carbon atoms, phenoxy, phenyl, thiophenoxy, benzoyl, benzyl, phenylamino, benzylamino, alkanoylamino of 1-6 carbon atoms, or alkyl of 1-6 carbon atoms;

R<sub>2</sub>, is selected from the group consisting of

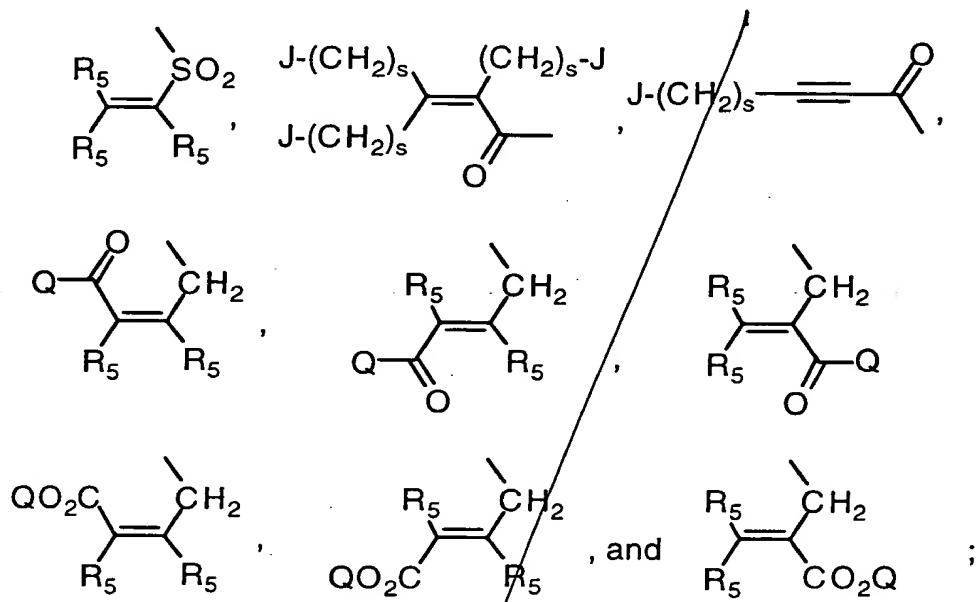
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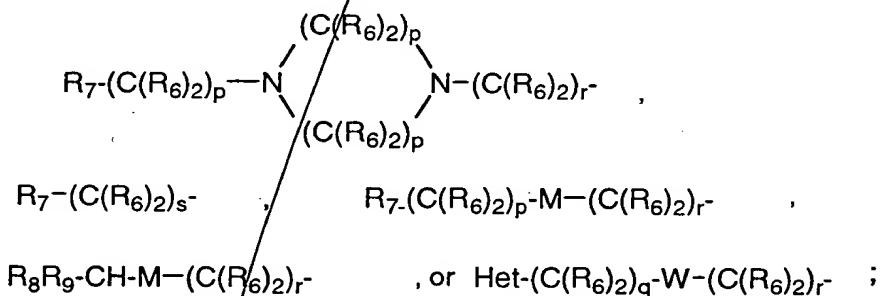
- 123 -



- 124 -

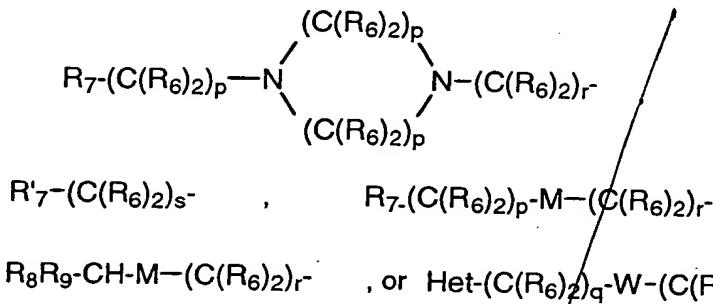


R<sub>3</sub> is independently hydrogen, alkyl of 1-6 carbon atoms, carboxy, carboalkoxy of 1-  
5 6 carbon atoms, phenyl, carboalkyl of 2-7 carbon atoms,



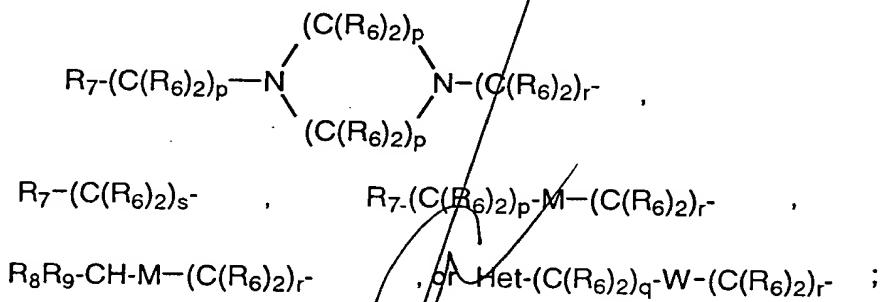
with the proviso that at least one of the R<sub>3</sub> groups is selected from the group

- 125 -



R<sub>5</sub> is independently hydrogen, alkyl of 1-6 carbon atoms, carboxy, carboalkoxy of 1-6 carbon atoms, phenyl, carboalkyl of 2-7 carbon atoms,

5



R<sub>8</sub>, and R<sub>9</sub> are each, independently,  $-(\text{C(R}_6\text{)}_2\text{)}_{\text{r}}\text{NR}_6\text{R}_6$ , or  $-(\text{C(R}_6\text{)}_2\text{)}_{\text{r}}\text{OR}_6$ ;

10

J is independently hydrogen, chlorine, fluorine, or bromine;

Q is alkyl of 1-6 carbon atoms or hydrogen;

a = 0 or 1;

g = 1-6;

15 k = 0-4;

n is 0-1;

p = 2-4;

q=0-4;

r = 1-4;

20 s = 1-6;

u = 0-4 and v = 0-4 , wherein the sum of u+v is 2-4;

- 126 -

or a pharmaceutically acceptable salt thereof,

provided that

when R<sub>6</sub> is alkenyl of 2-7 carbon atoms or alkynyl of 2-7 carbon atoms, such alkenyl or alkynyl moiety is bound to a nitrogen or oxygen atom through a saturated carbon atom;

and further provided that

when Y is -NR<sub>6</sub>- and R<sub>7</sub> is -NR<sub>6</sub>R<sub>6</sub>, -N(R<sub>6</sub>)<sub>3</sub><sup>+</sup>, or -NR<sub>6</sub>(OR<sub>6</sub>), then g = 2-6;

when M is -O- and R<sub>7</sub> is -OR<sub>6</sub>, then p = 1-4;

when Y is -NR<sub>6</sub>-, then k = 2-4;

when Y is -O- and M or W is -O-, then k = 1-4.

when W is not a bond with Het bonded through a nitrogen atom, then q = 2-4 and when W is a bond with Het bonded through a nitrogen atom and Y is -O- or -NR<sub>6</sub>-, then k = 2-4.

15 2. The compound according to claim 1 wherein Z is -NH- and n = 0 or a pharmaceutically acceptable salt thereof.

3. The compound according to claim 2 wherein X is optionally substituted phenyl or a pharmaceutically acceptable salt thereof.

20 4. The compound according to claim 3 wherein R<sub>1</sub> and R<sub>4</sub> are hydrogen or a pharmaceutically acceptable salt thereof.

5. The compound according to claim 1, which is:

25 a) 1-Methyl-1,2,5,6-tetrahydro-pyridine-3-carboxylic acid [4-(3-bromo-phenylamino)-3-cyano-quinolin-6-yl]-amide or a pharmaceutically acceptable salt thereof;

121

- 127 -

- b) N-[4-[(3-Bromophenyl)amino]-3-cyano-6-quinolinyl]-4-(N-allyl-N-methylamino)-2-butynamide or a pharmaceutically acceptable salt thereof;
- 5 c) N-[4-[(3-Bromophenyl)amino]-3-cyano-6-quinolinyl]-4-(N-methoxyethyl-N-methylamino)-2-butynamide or a pharmaceutically acceptable salt thereof;
- d) N-[4-[(3-Bromophenyl)amino]-3-cyano-6-quinolinyl]-4-(bis-(2-methoxyethyl)amino)-2-butynamide or a pharmaceutically acceptable salt thereof;
- 10 e) 4-Methoxymethoxy-but-2-yonoic acid [4-(3-bromo-phenylamino)-3-cyano-quinolin-6-yl]-amide or a pharmaceutically acceptable salt thereof;
- f) 4-(4-Chloro-2-fluoro-phenylamino)-6-methoxy-7-(2-pyridin-4-yl-ethoxy)-15 quinoline-3-carbonitrile or a pharmaceutically acceptable salt thereof;
- g) 4-(2-Methoxy-ethoxy)-but-2-yonoic acid [4-(3-bromo-phenylamino)-3- cyano-quinolin-6-yl]-amide or a pharmaceutically acceptable salt thereof;
- 20 h) 4-((2S)-2-Methoxymethylpyrrolidin-1-yl)but-2-yonoic Acid [4-(3-bromophenylamino)-3-cyanoquinolin-6-yl]amide or a pharmaceutically acceptable salt thereof;
- i) 4-(1,4-Dioxa-8-azaspiro[4,5]dec-8-yl)but-2-yonoic Acid [4-(3-25 Bromophenylamino)-3-cyanoquinolin-6-yl] amide or a pharmaceutically acceptable salt thereof;
- j) 4-(3-Bromo-phenylamino)-6-(2-ethoxy-3,4-dioxo-cyclobut-1-enylamino)-quinoline-3-carbonitrile or a pharmaceutically acceptable salt thereof;

122

128 -

- 5           k) 4-[(2-Methoxy-ethyl)-methyl-amino]-but-2-enoic acid [4-(3-chloro-4- fluoro-phenylamino)-3-cyano-7-methoxy-quinolin-6-yl]-amide or a pharmaceutically acceptable salt thereof;

10          l) (S)-4-(2-Methoxymethyl-pyrrolidin-1-yl)-but-2-enoic acid [4-(3-chloro-4- fluoro-phenylamino)-3-cyano-7-methoxy-quinolin-6-yl]-amide dihydrochloride or a pharmaceutically acceptable salt thereof;

15          m) 4-(3-Hydroxymethyl-piperidin-1-yl)-but-2-enoic acid [4-(3-chloro-4- fluoro-phenylamino)-3-cyano-7-methoxy-quinolin-6-yl]-amide or a pharmaceutically acceptable salt thereof;

20          n) 4-(1,4-Dioxa-8-aza-spiro[4.5]dec-8-yl)-but-2-enoic acid [4-(3- chloro-4- fluoro-phenylamino)-3-cyano-7-methoxy-quinolin-6-yl]-amide or a pharmaceutically acceptable salt thereof;

25          o) 4-(2-Hydroxymethyl-piperidin-1-yl)-but-2-enoic acid [4-(3-chloro-4- fluoro-phenylamino)-3-cyano-7-methoxy-quinolin-6-yl]-amide or a pharmaceutically acceptable salt thereof;

p) 4-Bromo-but-2-enoic acid [4-(3-chloro-4-fluoro-phenylamino)-3-cyano-7- methoxy-quinolin-6-yl]-amide or a pharmaceutically acceptable salt thereof;

q) 4-(3-hydroxy-4-methyl-phenylamino)-6-methoxy-7-(3-pyridin-4-yl-propoxy)- quinoline-3-carbonitrile or a pharmaceutically acceptable salt thereof;

r) 4-Diallylamino-but-2-enoic acid [4-(3-chloro-4-fluoro-phenylamino)- 3cyano-7-methoxy- quinolin-6-yl]-amide or a pharmaceutically acceptable salt thereof;

- 129 -

- s) 4-[Bis-(2-methoxy-ethyl)-amino]- but-2-enoic acid [4-(3-chloro-4-fluoro-phenylamino)- 3-cyano-7-methoxy-quinolin-6-yl]-amide or a pharmaceutically acceptable salt thereof;
- 5    t) 4-([1,3]Dioxolan-2-ylmethyl-methyl-amino)-but-2-enoic acid 3-cyano-7-methoxy -quinolin-6-yl]-amide or a pharmaceutically acceptable salt thereof;
- 10    u) 4-[Bis-(2-hydroxy-ethyl)-amino]-but-2-enoic acid [4-(3-chloro-4-fluoro-phenylamino)-3-cyano-7-methoxy- quinolin-6-yl]-amide or a pharmaceutically acceptable salt thereof;
- 15    v) 4-Thiomorpholin-4-yl-but-2-enoic acid [4-(3-chloro-4-fluoro-phenylamino)-3-cyano-7-methoxy-quinolin-6-yl]-amide or a pharmaceutically acceptable salt thereof;
- 20    w) 4-[4-(2-Hydroxy-ethyl)-piperazin-1-yl]-but-2-enoic acid [4-(3-chloro-4-fluoro-phenylamino)-3-cyano-7-methoxy- quinolin-6-yl]-amide or a pharmaceutically acceptable salt thereof;
- 25    x) 4-(1,4,7-Trioxa-10-aza-cyclododec-10-yl)-but-2-enoic acid [4-(3-chloro-4-fluoro-phenylamino)-3-cyano-7-methoxy- quinolin-6-yl]-amide or a pharmaceutically acceptable salt thereof;
- 30    y) 4-(Methoxy-methyl-amino)-but-2-enoic acid [4-(3-chloro-4-fluoro-phenylamino)-3-cyano-7-methoxy-quinolin-6-yl]-amide or a pharmaceutically acceptable salt thereof;
- z) 4-(4-Hydroxy-piperidin-1-yl)-but-2-enoic acid [4-(3-chloro-4-fluoro-phenylamino)-3-cyano-7-methoxy-quinolin-6-yl]-amide or a pharmaceutically acceptable salt thereof;

124

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- aa) 4-[1,4']Bipiperidinyl-1'-yl-but-2-enoic acid [4-(3-chloro-4-fluoro-phenylamino)-3-cyano-7-methoxy-quinolin-6-yl]-amide or a pharmaceutically acceptable salt thereof;
- 5 bb) 4-Thiazolidin-3-yl-but-2-enoic acid [4-(3-chloro-4-fluoro-phenylamino)-3-cyano-7-methoxy-quinolin-6-yl]-amide or a pharmaceutically acceptable salt thereof;
- 10 cc) 3-{3-[4-(3-Chloro-4-fluoro-phenylamino)-3-cyano-7-methoxy-quinolin-6-ylcarbamoyl]-allyl}-4-methyl-thiazol-3-i um bromide or a pharmaceutically acceptable salt thereof;
- 15 dd) 4-(2,6-Dimethyl-piperidin-1-yl)-but-2-enoic acid [4-(3-chloro-4-fluoro-phenylamino)-3-cyano-7-methoxy-quinolin-6-yl]-amide or a pharmaceutically acceptable salt thereof;
- ee) 4-[Bis-(2-hydroxy-propyl)-amino]-but-2-enoic acid [4-(3-chloro-4-fluoro-phenylamino)-3-cyano-7-methoxy-quinolin-6-yl]-amide or a pharmaceutically acceptable salt thereof;
- 20 ff) 4-(3-Hydroxy-pyrrolidin-1-yl)-but-2-enoic acid [4-(3-chloro-4-fluoro-phenylamino)-3-cyano-7-methoxy-quinolin-6-yl]-amide or a pharmaceutically acceptable salt thereof;
- 25 gg) 4-[(2-Hydroxy-ethyl)-methyl-amino]-but-2-enoic acid [4-(3-chloro-4-fluoro-phenylamino)-3-cyano-7-methoxy-quinolin-6-yl]-amide or a pharmaceutically acceptable salt thereof;

125

- hh) 4-(2,5-Dimethyl-pyrrolidin-1-yl)-but-2-enoic acid [4-(3-chloro-4-fluoro-phenylamino)-3-cyano-7-methoxy-quinolin-6-yl]-amide or a pharmaceutically acceptable salt thereof;
- 5    ii) 4-(4,4-Dihydroxy-piperidin-1-yl)-but-2-enoic acid [4-(3-chloro-4-fluoro-phenylamino)-3-cyano-7-methoxy-quinolin-6-yl]-amide or a pharmaceutically acceptable salt thereof;
- jj) 4-(3-Chloro-4-fluoro-phenylamino)-7-methoxy-6-pyrrolidin-1-yl-quinoline-3-carbonitrile or a pharmaceutically acceptable salt thereof;
- 10    kk) 4-(3-Chloro-4-fluoroanilino)-7-methoxy-6-(1H-pyrrol-1-yl)-3-quinolinecarbonitrile or a pharmaceutically acceptable salt thereof;
- 15    ll) 6-(1-Aziridinyl)-4-(3-chloro-4-fluoroanilino)-7-methoxy-3-quinolinecarbonitrile or a pharmaceutically acceptable salt thereof;
- mm) 4-[(2-Methoxy-ethyl)-methyl-amino]-but-2-enoic acid [4-(3-bromo-phenylamino)-3-cyano-7-ethoxy-quinolin-6-yl]-amide or a pharmaceutically acceptable salt thereof;
- 20    nn) 4-(2,4-Dichloro-5-methoxy-phenylamino)-7-[3-(4-hydroxy-piperidin-1-yl)-propoxy]-6-methoxy-quinoline-3-carbonitrile or a pharmaceutically acceptable salt thereof;
- 25    oo) 4-(2,4-Dichloro-5-methoxy-phenylamino)-7-{3-[4-(2-hydroxy-ethyl)-piperazin-1-yl]-propoxy}-6-methoxy-quinoline-3-carbonitrile or a pharmaceutically acceptable salt thereof;

126

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- pp) 4-(2-Bromo-4-chloro-phenylamino)-7-{2-[(2-hydroxy-ethyl)-methyl-amino]-ethoxy}-6-methoxy-quinoline-3-carbonitrile or a pharmaceutically acceptable salt thereof;
- 5 qq) 4-(2,4-Dichloro-5-methoxy-phenylamino)-7-{3-[(2-hydroxy-ethyl)-methyl-amino]-propoxy}-6-methoxy-quinoline-3-carbonitrile or a pharmaceutically acceptable salt thereof;
- 10 rr) 4-(2,4-Dichloro-5-methoxy-phenylamino)-6-methoxy-7-(3-thiomorpholin-4-yl-propoxy)-quinoline-3-carbonitrile or a pharmaceutically acceptable salt thereof;
- 15 ss) 4-(2,4-Dichloro-5-methoxy-phenylamino)-6-methoxy-7-[3-(2-methoxy-ethylamino)-propoxy]-quinoline-3-carbonitrile or a pharmaceutically acceptable salt thereof;
- 20 tt) 4-(2,4-Dichloro-5-methoxy-phenylamino)-6-methoxy-7-[3-(4-methyl-piperidin-1-yl)-propoxy]-quinoline-3-carbonitrile or a pharmaceutically acceptable salt thereof;
- uu) 4-(2,4-Dichloro-5-methoxy-phenylamino)-7-[3-(2,6-dimethyl-morpholin-4-yl)-propoxy]-6-methoxy-quinoline-3-carbonitrile or a pharmaceutically acceptable salt thereof;
- 25 vv) 4-(2-Bromo-4-chloro-phenylamino)-7-{2-[4-(2-hydroxy-ethyl)-piperazin-1-yl]-ethoxy}-6-methoxy-quinoline-3-carbonitrile or a pharmaceutically acceptable salt thereof;
- ww) 4-(2-Bromo-4-chloro-phenylamino)-7-[2-(4-hydroxy-piperidin-1-yl)-ethoxy]-6-methoxy-quinoline-3-carbonitrile or a pharmaceutically acceptable salt thereof;

- xx) 4-(2-Bromo-4-chloro-phenylamino)-6-methoxy-7-(2-thiomorpholin-4-yl-  
ethoxy)-quinoline-3-carbonitrile or a pharmaceutically acceptable salt thereof;
- 5 yy) 4-(2,4-Dichloro-5-methoxy-phenylamino)-7-[3-(2,5-dimethyl-pyrrolidin-1-  
yl)-propoxy]-6-methoxy-quinoline-3-carbonitrile or a pharmaceutically  
acceptable salt thereof;
- 10 zz) 4-(2,4-Dichloro-5-methoxy-phenylamino)-7-[3-(3-hydroxy-propylamino)-  
propoxy]-6-methoxy-quinoline-3-carbonitrile or a pharmaceutically  
acceptable salt thereof;
- 15 aaa) 1-{3-[3-Cyano-4-(2,4-dichloro-5-methoxy-phenylamino)-6-methoxy-  
quinolin-7-yloxy]-propyl}-piperidine-4-carboxylic acid ethyl ester or a  
pharmaceutically acceptable salt thereof;
- 20 bbb) 7-[3-(4-acetyl-1-piperazinyl)propoxy]-4-[(2,4-dichloro-5-  
methoxyphenyl)amino]-6-methoxy-3-quinolinecarbonitrile or a  
pharmaceutically acceptable salt thereof;
- ccc) 4-(3-chloro-4-fluoroanilino)-7-methoxy-6(4-morpholinyl)-3-  
quinolinecarbonitrile or a pharmaceutically acceptable salt thereof;
- 25 ddd) 7-[3-(4-Benzyl-piperazin-1-yl)-propoxy]-4-(2,4-dichloro-5-methoxy-  
phenylamino)-6-methoxy-quinoline-3-carbonitrile or a pharmaceutically  
acceptable salt thereof;
- eee) 4-(2,4-Dichloro-5-methoxy-phenylamino)-7-[3-(2-hydroxy-ethylamino)-  
propoxy]-6-methoxy-quinoline-3-carbonitrile or a pharmaceutically  
acceptable salt thereof;

- fff) 4-(2,4-Dichloro-5-methoxy-phenylamino)-7-{3-[ethyl-(2-hydroxy-ethyl)-amino]-propoxy}-6-methoxy-quinoline-3-carbonitrile or a pharmaceutically acceptable salt thereof;
- 5 5 ggg) 7-{3-[Bis-(2-methoxy-ethyl)-amino]-propoxy}-4-(2,4-dichloro-5-methoxy-phenylamino)-6-methoxy-quinoline-3-carbonitrile or a pharmaceutically acceptable salt thereof;
- 10 hhh) 7-{3-[Bis-(2-hydroxy-ethyl)-amino]-propoxy}-4-(2,4-dichloro-5-methoxy-phenylamino)-6-methoxy-quinoline-3-carbonitrile or a pharmaceutically acceptable salt thereof;
- 15 iii) 4-(3-chloro-4-fluoroanilino)-7-(4-morpholinyl)-6-nitro-3-quinolinecarbonitrile or a pharmaceutically acceptable salt thereof;
- jjj) N-[4-(3-chloro-4-fluoroanilino)-3-cyano-7-(4-morpholinyl)-6-quinolinyl]-2-butynamide or a pharmaceutically acceptable salt thereof;
- 20 kkk) 6-amino-4-(3-chloro-4-fluoroanilino)-7-(4-morpholinyl)-3-quinolinecarbonitrile or a pharmaceutically acceptable salt thereof;
- lll) 4-(2,4-dichloro-5-methoxyanilino)-6-methoxy-7-(3-{[2-(4--morpholinyl)ethyl]amino}propoxy)-3-quinolinecarbonitrile or a pharmaceutically acceptable salt thereof;
- 25 mmm) 7-{3-[(2-anilinoethyl)amino]propoxy}-4-(2,4-dichloro-5-methoxyanilino)-6-methoxy-3-quinolinecarbonitrile or a pharmaceutically acceptable salt thereof;
- nnn) N-[4-(3-chloro-4-fluoroanilino)-3-cyano-7-(4-morpholinyl)-6-quinolinyl]acrylamide or a pharmaceutically acceptable salt thereof;

129

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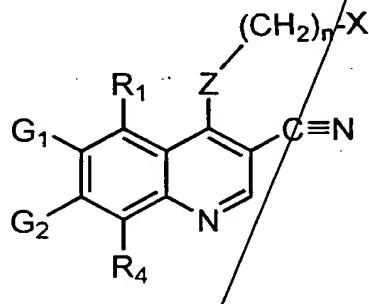
- ooo) 4-(3-chloro-4-fluoroanilino)-7-{4-[2-(dimethylamino)ethyl]-1-piperazinyl}-6-nitro-3-quinolinecarbonitrile or a pharmaceutically acceptable salt thereof;
- 5 ppp) 6-amino-4-(3-chloro-4-fluoroanilino)-7-{4-[2-(dimethylamino)ethyl]-1-piperazinyl}-3-quinolinecarbonitrile or a pharmaceutically acceptable salt thereof;
- 10 qqq) N-(4-(3-chloro-4-fluoroanilino)-3-cyano-7-{4-[2-(dimethylamino)ethyl]-1-piperazinyl}-6-quinolinyl)acrylamide or a pharmaceutically acceptable salt thereof;
- 15 rr) 4-(2,4-dichloro-5-methoxyanilino)-6-methoxy-7-({2-[4-(2-methoxyethyl)-1-piperazinyl]ethyl}amino)-3-quinolinecarbonitrile or a pharmaceutically acceptable salt thereof;
- 20 sss) 4-(2,4-dichloro-5-methoxyanilino)-6-methoxy-7-[3-(2H-1,2,3-triazol-2-yl)propoxy]-3-quinolinecarbonitrile or a pharmaceutically acceptable salt thereof;
- 25 ttt) 4-(2,4-dichloro-5-methoxyanilino)-6-methoxy-7-[3-(1H-1,2,3-triazol-1-yl)propoxy]-3-quinolinecarbonitrile or a pharmaceutically acceptable salt thereof;
- uuu) 4-(2,4-dichloro-5-methoxyanilino)-6-methoxy-7-(3-thienyl)-3-quinolinecarbonitrile or a pharmaceutically acceptable salt thereof;
- 27 vvv) 4-[(E)-2-(2-quinolinyl)ethenyl]aniline or a pharmaceutically acceptable salt thereof;

- www) 4-(2,4-dichloro-5-methoxyanilino)-6-methoxy-7-{{2-(2H-1,2,3-triazol-2-yl)ethyl]amino}-3-quinolinecarbonitrile or a pharmaceutically acceptable salt thereof;
- 5 5 xxx) 4-(2,4-dichloro-5-methoxyanilino)-6-methoxy-7-{{2-(1H-1,2,3-triazol-1-yl)ethyl]amino}-3-quinolinecarbonitrile or a pharmaceutically acceptable salt thereof;
- 10 10 yyy) 4-(2,4-dichloro-5-methoxyanilino)-7-(3-thienyl)-3-quinolinecarbonitrile or a pharmaceutically acceptable salt thereof;
- 15 15 zzz) 4-(2,4-dichloro-5-methoxyanilino)-6-methoxy-7-[3-(1H-1,2,4-triazol-1-yl)propoxy]-3-quinolinecarbonitrile or a pharmaceutically acceptable salt thereof;
- aaaa) 4-(2,4-dichloro-5-methoxyanilino)-7-[3-(1H-imidazol-1-yl)propoxy]-6-methoxy-3-quinolinecarbonitrile or a pharmaceutically acceptable salt thereof;
- 20 20 bbbb) 4-(2,4-dichloro-5-methoxyanilino)-6-methoxy-7-[3-(1H-pyrazol-1-yl)propoxy]-3-quinolinecarbonitrile or a pharmaceutically acceptable salt thereof;
- 25 25 cccc) N-[3-cyano-4-(2,4-dichloro-5-methoxyanilino)-6-methoxy-7-quinolinyl]-N-[4-(4-ethyl-1-piperazinyl)butyl]acetamide or a pharmaceutically acceptable salt thereof;
- 30 dddd) N-[3-cyano-4-(2,4-dichloro-5-methoxyanilino)-6-methoxy-7-quinolinyl]-N-(3-(4-ethyl-1-piperazinyl)propyl)acetamide or a pharmaceutically acceptable salt thereof;

- eeee) 4-(2,4-dichloro-5-methoxyanilino)-6-methoxy-7-{3-[4-(2-methoxyethyl)-1-piperazinyl]propoxy}-3-quinolinecarbonitrile or a pharmaceutically acceptable salt thereof;
- 5 ffff) 4-(2,4-dichloro-5-methoxyanilino)-6-methoxy-7-(1H-pyrrol-1-yl)-3-quinolinecarbonitrile or a pharmaceutically acceptable salt thereof;
- 10 gggg) 4-(4-bromo-2-fluoroanilino)-6-methoxy-7-[2-(1H-1,2,3-triazol-1-yl)ethoxy]-3-quinolinecarbonitrile or a pharmaceutically acceptable salt thereof;
- 15 hhhh) 4-(4-bromo-2-fluoroanilino)-6-methoxy-7-[2-(2H-1,2,3-triazol-2-yl)ethoxy]-3-quinolinecarbonitrile or a pharmaceutically acceptable salt thereof;
- iiii) '4-(2,4-dichloro-5-methoxyanilino)-6-methoxy-7-[3-(1H-tetraazol-1-yl)propoxy]-3-quinolinecarbonitrile or a pharmaceutically acceptable salt thereof;
- 20 jjjj) 4-(2,4-dichloro-5-methoxyanilino)-6-methoxy-7-[3-(2H-tetraazol-2-yl)propoxy]-3-quinolinecarbonitrile or a pharmaceutically acceptable salt thereof;
- kkkk) 4-(4-bromo-2-fluoroanilino)-6-methoxy-7-[2-(1H-1,2,3-triazol-1-yl)ethoxy]-3-quinolinecarbonitrile or a pharmaceutically acceptable salt thereof;
- 25 llll) 4-(4-bromo-2-fluoroanilino)-6-methoxy-7-[2-(2H-1,2,3-triazol-2-yl)ethoxy]-3-quinolinecarbonitrile or a pharmaceutically acceptable salt thereof; or
- 30 mmmm) 4-(2,4-dichloro-5-methoxyanilino)-7-{3-[[2-(dimethylamino)ethyl](methyl)amino]propoxy}-6-methoxy-3-quinolinecarbonitrile or a pharmaceutically acceptable salt thereof.

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6. A method of treating, inhibiting the growth of, or eradicating a neoplasm in a mammal in need thereof which comprises administering to said mammal an effective amount of a compound of formula 1 having the structure



5

wherein:

X is cycloalkyl of 3 to 7 carbon atoms, which may be optionally substituted with one or more alkyl of 1 to 6 carbon atom groups; or is a pyridinyl, pyrimidinyl, or phenyl ring wherein the pyridinyl, pyrimidinyl, or phenyl ring may be optionally mono-, di-, or tri-substituted with a substituent selected from the group consisting of halogen, alkyl of 1-6 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl of 2-6 carbon atoms, azido, hydroxyalkyl of 1-6 carbon atoms, halomethyl, alkoxymethyl of 2-7 carbon atoms, alkanoyloxymethyl of 2-7 carbon atoms, alkoxy of 1-6 carbon atoms, alkylthio of 1-6 carbon atoms, hydroxy, trifluoromethyl, cyano, nitro, carboxy, carboalkoxy of 2-7 carbon atoms, carboalkyl of 2-7 carbon atoms, phenoxy, phenyl, thiophenoxy, benzoyl, benzyl, amino, alkylamino of 1-6 carbon atoms, dialkylamino of 2 to 12 carbon atoms, phenylamino, benzylamino, alkanoylamino of 1-6 carbon atoms, alkenoylamino of 3-8 carbon atoms, alkynoylamino of 3-8 carbon atoms, carboxyalkyl of 2-7 carbon atoms, carboalkoxyalkyl of 3-8 carbon atoms, aminoalkyl of 1-5 carbon atoms, N-alkylaminoalkyl of 2-9 carbon atoms, N,N-dialkylaminoalkyl of 3-10 carbon atoms, N-alkylaminoalkoxy of 2-9 carbon atoms, N,N-dialkylaminoalkoxy of 3-10 carbon atoms, mercapto, and benzoylamino;

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Z is -NH-, -O-, -S-, or -NR- ;

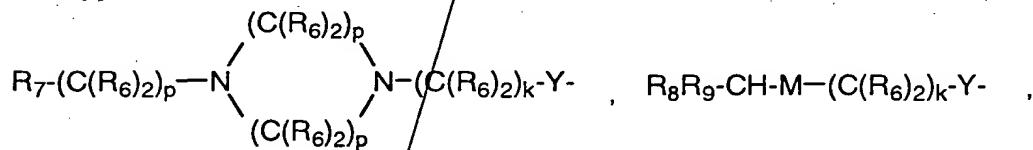
R is alkyl of 1-6 carbon atoms, or carboalkyl of 2-7 carbon atoms;

G<sub>1</sub>, G<sub>2</sub>, R<sub>1</sub>, and R<sub>4</sub> are each, independently, hydrogen, halogen, alkyl of 1-6 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl of 2-6 carbon atoms, alkenyloxy

5 of 2-6 carbon atoms, alkynyloxy of 2-6 carbon atoms, hydroxymethyl, halomethyl, alkanoyloxy of 1-6 carbon atoms, alkenoyloxy of 3-8 carbon atoms, alkynoyloxy of 3-8 carbon atoms, alkanoyloxymethyl of 2-7 carbon atoms, alkenoyloxymethyl of 4-9 carbon atoms, alkynoyloxymethyl of 4-9 carbon atoms, alkoxymethyl of 2-7 carbon atoms, alkoxy of 1-6 carbon atoms.

10 alkylthio of 1-6 carbon atoms, alkylsulphanyl of 1-6 carbon atoms,  
alkylsulphonyl of 1-6 carbon atoms, alkylsulfonamido of 1-6 carbon atoms,  
alkenylsulfonamido of 2-6 carbon atoms, alkynylsulfonamido of 2-6 carbon  
atoms, hydroxy, trifluoromethyl, trifluoromethoxy, cyano, nitro, carboxy,  
carboalkoxy of 2-7 carbon atoms, carboalkyl of 2-7 carbon atoms, phenoxy,  
phenyl, thiophenoxy, benzyl, amino, hydroxyamino, alkoxyamino of 1-4  
carbon atoms, alkylamino of 1-6 carbon atoms, dialkylamino of 2 to 12  
carbon atoms, N-alkylcarbamoyl, N,N-dialkylcarbamoyl, N-alkyl-N-  
alkenylamino of 4 to 12 carbon atoms, N,N-dialkenylamino of 6-12 carbon  
atoms, phenylamino, benzylamino,

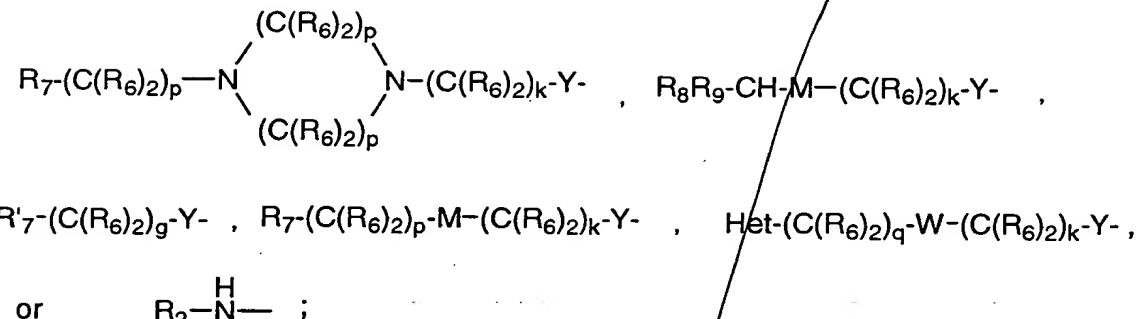
20



$R_7-(C(R_6)_2)_g-Y-$ ,  $R_7-(C(R_6)_2)_p-M-(C(R_6)_2)_k-Y-$ , or  $Het-(C(R_6)_2)_q-W-(C(R_6)_2)_k-Y-$

with the proviso that either G<sub>1</sub> or G<sub>2</sub> or both G<sub>1</sub> and G<sub>2</sub> must be a radical selected from the group

- 140 -



Y is a divalent radical selected from the group consisting of

$-(CH_2)_a-$ ,  $-O-$ , and  $-N(R_6)-$

R<sub>7</sub> is -NR<sub>6</sub>R<sub>6</sub>, -J, -OR<sub>6</sub>, -N(R<sub>6</sub>)<sub>3</sub><sup>+</sup>, or -NR<sub>6</sub>(OR<sub>6</sub>)<sub>2</sub>;

R'7 is -NR<sub>6</sub>(OR<sub>6</sub>), -N(R<sub>6</sub>)<sub>3</sub><sup>+</sup>, alkoxy of 1-6 carbon atoms, alkynoxy of 1-6 carbon atoms, N-alkyl-N-alkenylamino of 4 to 12 carbon atoms, N,N-dialkenylamino of 6-12 carbon atoms, N-alkyl-N-alkynylamino of 4 to 12 carbon atoms, N-alkenyl-N-alkynylamino of 4 to 12 carbon atoms, or N,N-dialkynylamino of 6-12 carbon atoms with the proviso that the alkenyl or alkynyl moiety is bound to a nitrogen or oxygen atom through a saturated carbon atom;

M is  $>\text{NR}_6$ ,  $-\text{O}-$ ,  $>\text{N}-(\text{C}(\text{R}_6)_2)_p\text{NR}_6\text{R}_6$  or  $>\text{N}-(\text{C}(\text{R}_6)_2)_p-\text{OR}_6$ ;

15 W is >NR<sub>6</sub>, -O- or is a bond;

Het is a heterocycle selected from the group consisting of morpholine, thiomorpholine, thiomorpholine S-oxide, thiomorpholine S,S-dioxide, piperidine, pyrrolidine, aziridine, pyridine, imidazole, 1,2,3-triazole, 1,2,4-triazole, thiazole, thiazolidine, tetrazole, piperazine, furan, thiophene, tetrahydrothiophene, tetrahydrofuran, dioxane, 1,3-dioxolane,

tetrahydropyran, and

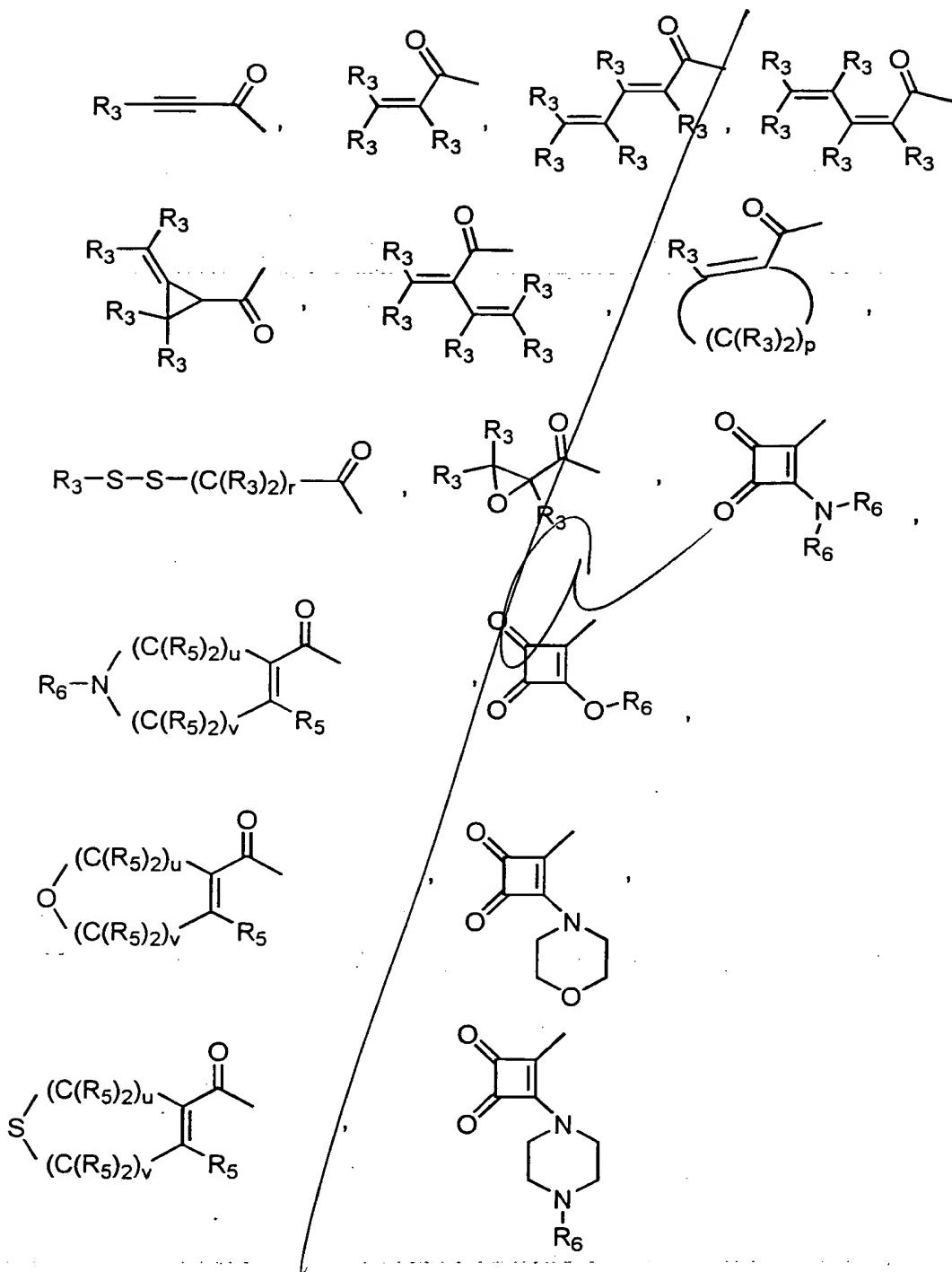
- 141 -

wherein the heterocycle is optionally mono- or di-substituted on carbon or nitrogen with R<sub>6</sub>, optionally mono- or di-substituted on carbon with hydroxy, -N(R<sub>6</sub>)<sub>2</sub>, or -OR<sub>6</sub>, optionally mono or di-substituted on carbon with the mono-valent radicals -(C(R<sub>6</sub>)<sub>2</sub>)<sub>s</sub>OR<sub>6</sub> or -(C(R<sub>6</sub>)<sub>2</sub>)<sub>s</sub>N(R<sub>6</sub>)<sub>2</sub>, or optionally 5 mono or di-substituted on a saturated carbon with divalent radicals -O- or -O(C(R<sub>6</sub>)<sub>2</sub>)<sub>s</sub>O-;

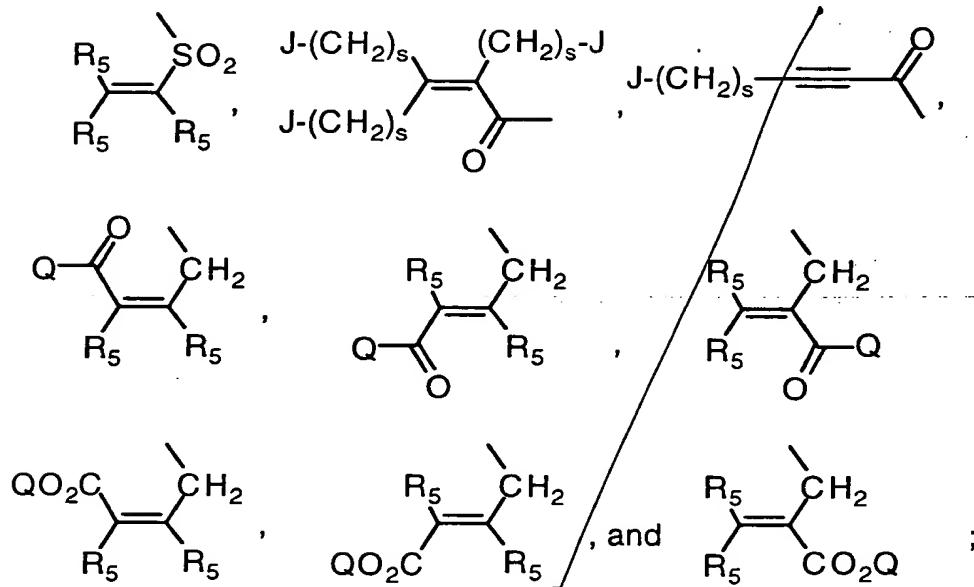
R<sub>6</sub> is hydrogen, alkyl of 1-6 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl of 2-6 carbon atoms, cycloalkyl of 1-6 carbon atoms, carboalkyl of 2-7 carbon 10 atoms, carboxyalkyl (2-7 carbon atoms), phenyl, or phenyl optionally substituted with one or more halogen, alkoxy of 1-6 carbon atoms, trifluoromethyl, amino, alkylamino of 1-3 carbon atoms, dialkylamino of 2-6 carbon atoms, nitro, cyano, azido, halomethyl, alkoxymethyl of 2-7 carbon atoms, alkanoyloxymethyl of 2-7 carbon atoms, alkylthio of 1-6 carbon 15 atoms, hydroxy, carboxyl, carboalkoxy of 2-7 carbon atoms, phenoxy, phenyl, thiophenoxy, benzoyl, benzyl, phenylamino, benzylamino, alkanoylamino of 1-6 carbon atoms, or alkyl of 1-6 carbon atoms;

R<sub>2</sub>, is selected from the group consisting of 20

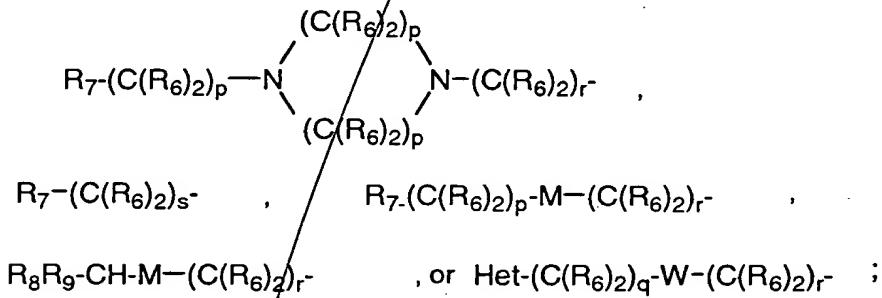
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- 143 -

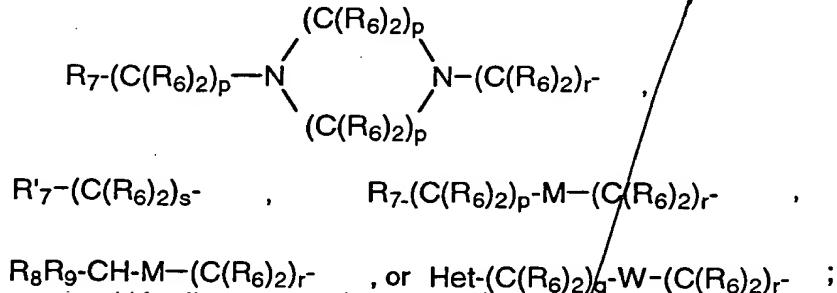


R<sub>3</sub> is independently hydrogen, alkyl of 1-6 carbon atoms, carboxy, carboalkoxy of 1-5 carbon atoms, phenyl, carboalkyl of 2-7 carbon atoms,



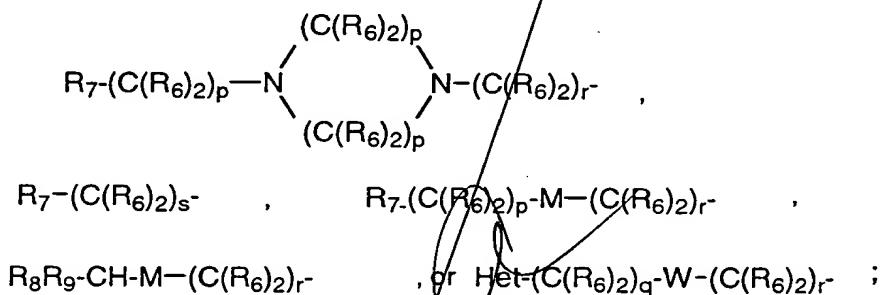
with the proviso that at least one of the R<sub>3</sub> groups is selected from the group

144 -



R5 is independently hydrogen, alkyl of 1-6 carbon atoms, carboxy, carboalkoxy of 1-6 carbon atoms, phenyl, carboalkyl of 2-7 carbon atoms,

5



R<sub>8</sub>, and R<sub>9</sub> are each, independently, -(C(R<sub>6</sub>)<sub>2</sub>)<sub>r</sub>NR<sub>6</sub>R<sub>6</sub>, or -(C(R<sub>6</sub>)<sub>2</sub>)<sub>r</sub>OR<sub>6</sub>;

10

J is independently hydrogen, chlorine, fluorine, or bromine;

Q is alkyl of 1-6 carbon atoms or hydrogen;

$$a = 0 \text{ or } 1;$$

$g = 1-6;$

15 k = 0-4;

n is 0-1;

p = 2-4;

q=0-4;

r = 1-4;

20       $s = 1-6;$

$u = 0-4$  and  $v = 0-4$ , wherein the sum of  $u+v$  is  $2-4$ ;

or a pharmaceutically acceptable salt thereof,  
provided that

when R<sub>6</sub> is alkenyl of 2-7 carbon atoms or alkynyl of 2-7 carbon atoms, such  
alkenyl or alkynyl moiety is bound to a nitrogen or oxygen atom  
through a saturated carbon atom;

and further provided that

when Y is -NR<sub>6</sub>- and R<sub>7</sub> is NR<sub>6</sub>R<sub>6</sub>, -N(R<sub>6</sub>)<sub>3</sub><sup>+</sup>, or -NR<sub>6</sub>(OR<sub>6</sub>), then g = 2-6;

when M is -O- and R<sub>7</sub> is OR<sub>6</sub>, then p = 1-4;

when Y is -NR<sub>6</sub>-, then k = 2-4,

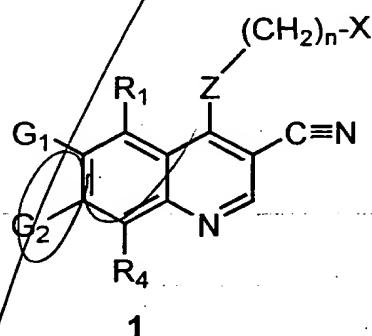
when Y is -O- and M or W is -O-, then k = 1-4

when W is not a bond with Het bonded through a nitrogen atom, then q = 2-4

and when W is a bond with Het bonded through a nitrogen atom and Y is -O- or -NR<sub>6</sub>-, then k = 2-4

15 7. The method according to claim 6 wherein the neoplasm is selected from the group consisting of breast, kidney, bladder, mouth, larynx, esophagus, stomach, colon, ovary, and lung.

20 8. A method of treating, inhibiting the progression of, or eradicating polycystic kidney disease in a mammal in need thereof which comprises administering to said mammal an effective amount of a compound of formula 1 having the structure



25 wherein:

- 146 -

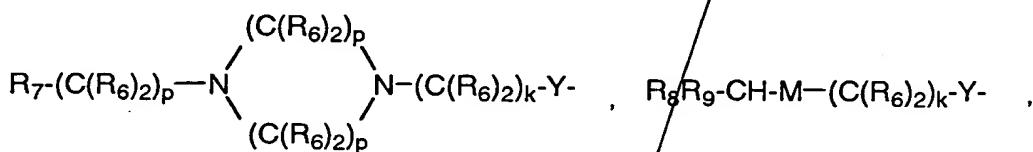
X is cycloalkyl of 3 to 7 carbon atoms, which may be optionally substituted with one or more alkyl of 1 to 6 carbon atom groups; or is a pyridinyl, pyrimidinyl, or phenyl ring wherein the pyridinyl, pyrimidinyl, or phenyl ring may be optionally mono-, di-, or tri-substituted with a substituent selected from the group consisting of halogen, alkyl of 1-6 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl of 2-6 carbon atoms, azido, hydroxyalkyl of 1-6 carbon atoms, halomethyl, alkoxymethyl of 2-7 carbon atoms, alkanoyloxymethyl of 2-7 carbon atoms, alkoxy of 1-6 carbon atoms, alkylthio of 1-6 carbon atoms, hydroxy, trifluoromethyl, cyano, nitro, carboxy, carboalkoxy of 2-7 carbon atoms, carboalkyl of 2-7 carbon atoms, phenoxy, phenyl, thiophenoxy, benzoyl, benzyl, amino, alkylamino of 1-6 carbon atoms, dialkylamino of 2 to 12 carbon atoms, phenylamino, benzylamino, alkanoylamino of 1-6 carbon atoms, alkenoylamino of 3-8 carbon atoms, alkynoylamino of 3-8 carbon atoms, carboxyalkyl of 2-7 carbon atoms, carboalkoxyalkyl of 3-8 carbon atoms, aminoalkyl of 1-5 carbon atoms, N-alkylaminoalkyl of 2-9 carbon atoms, N,N-dialkylaminoalkyl of 3-10 carbon atoms, N-alkylaminoalkoxy of 2-9 carbon atoms, N,N-dialkylaminoalkoxy of 3-10 carbon atoms, mercapto, and benzoylamino;

Z is -NH-, -O-, -S-, or -NR- ;

20 R is alkyl of 1-6 carbon atoms, or carboalkyl of 2-7 carbon atoms;

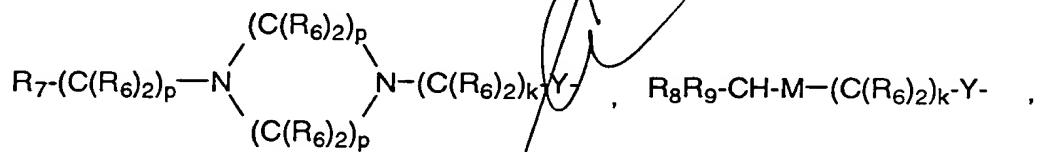
G<sub>1</sub>, G<sub>2</sub>, R<sub>1</sub>, and R<sub>4</sub> are each, independently, hydrogen, halogen, alkyl of 1-6 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl of 2-6 carbon atoms, alkenyloxy of 2-6 carbon atoms, alkynyloxy of 2-6 carbon atoms, hydroxymethyl, halomethyl, alkanoyloxy of 1-6 carbon atoms, alkenoyloxy of 3-8 carbon atoms, alkynoyloxy of 3-8 carbon atoms, alkanoyloxymethyl of 2-7 carbon atoms, alkenoyloxymethyl of 4-9 carbon atoms, alkoxymethyl of 2-7 carbon atoms, alkoxy of 1-6 carbon atoms, alkylthio of 1-6 carbon atoms, alkylsulphinyl of 1-6 carbon atoms, alkylsulphonyl of 1-6 carbon atoms, alkylsulfonamido of 1-6 carbon atoms, alkenylsulfonamido of 2-6 carbon atoms, alkynylsulfonamido of 2-6 carbon atoms, hydroxy, trifluoromethyl, trifluoromethoxy, cyano, nitro, carboxy,

carboalkoxy of 2-7 carbon atoms, carboalkyl of 2-7 carbon atoms, phenoxy, phenyl, thiophenoxy, benzyl, amino, hydroxyamino, alkoxyamino of 1-4 carbon atoms, alkylamino of 1-6 carbon atoms, dialkylamino of 2 to 12 carbon atoms, N-alkylcarbamoyl, N,N-dialkylcarbamoyl, N-alkyl-N-5 alkenylamino of 4 to 12 carbon atoms, N,N-dialkenylamino of 6-12 carbon atoms, phenylamino, benzylamino,



$R_7-(C(R_6)_2)_q-Y-$ ,  $R_7-(C(R_6)_2)_p-M-(C(R_6)_2)_k-Y-$ , or  $\text{Het}-(C(R_6)_2)_q-W-(C(R_6)_2)_k-Y-$

with the proviso that either  $G_1$  or  $G_2$  or both  $G_1$  and  $G_2$  must be a radical  
10 selected from the group

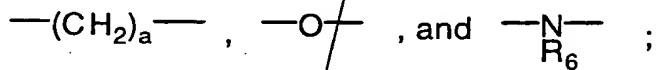


$R'_7-(C(R_6)_2)_q-Y-$ ,  $R_7-(C(R_6)_2)_p-M-(C(R_6)_2)_k-Y-$ ,  $\text{Het}-(C(R_6)_2)_q-W-(C(R_6)_2)_k-Y-$ ,

or  $R_2-\overset{H}{N}-$  ;

Y is a divalent radical selected from the group consisting of

15



$R_7$  is  $-\text{NR}_6\text{R}_6$ ,  $-\text{J}$ ,  $-\text{OR}_6$ ,  $-\text{N}(\text{R}_6)_3^+$ , or  $-\text{NR}_6(\text{OR}_6)$ ;

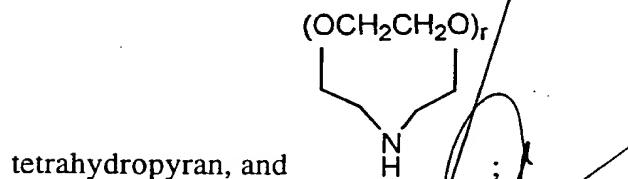
$R'_7$  is  $-\text{NR}_6(\text{OR}_6)$ ,  $-\text{N}(\text{R}_6)_3^+$ , alkoxy of 1-6 carbon atoms, alkynoxy of 1-6 carbon  
20 atoms, N-alkyl-N-alkenylamino of 4 to 12 carbon atoms, N,N-dialkenylamino of 6-12 carbon atoms, N-alkyl-N-alkynylamino of 4 to 12 carbon atoms, N-alkenyl-N-

alkynylamino of 4 to 12 carbon atoms, or N,N-dialkynylamino of 6-12 carbon atoms with the proviso that the alkenyl or alkynyl moiety is bound to a nitrogen or oxygen atom through a saturated carbon atom;

M is  $>\text{NR}_6$ ,  $-\text{O}-$ ,  $>\text{N}-(\text{C}(\text{R}_6)_2)_p\text{NR}_6\text{R}_6$ , or  $>\text{N}-(\text{C}(\text{R}_6)_2)_p-\text{OR}_6$ ;

5 W is  $>\text{NR}_6$ ,  $-\text{O}-$  or is a bond;

Het is a heterocycle selected from the group consisting of morpholine, thiomorpholine, thiomorpholine S-oxide, thiomorpholine S,S-dioxide, piperidine, pyrrolidine, aziridine, pyridine, imidazole, 1,2,3-triazole, 1,2,4-triazole, thiazole, thiazolidine, tetrazole, piperazine, furan, thiophene, 10 tetrahydrothiophene, tetrahydrofuran, dioxane, 1,3-dioxolane ,



tetrahydropyran, and

wherein the heterocycle is optionally mono- or di-substituted on carbon or nitrogen with  $\text{R}_6$ , optionally mono- or di-substituted on carbon with hydroxy,  $-\text{N}(\text{R}_6)_2$ , or  $-\text{OR}_6$ , optionally mono or di-substituted on carbon with the mono-valent radicals  $-(\text{C}(\text{R}_6)_2)_s\text{OR}_6$  or  $-(\text{C}(\text{R}_6)_2)_s\text{N}(\text{R}_6)_2$ , or optionally 15 mono or di-substituted on a saturated carbon with divalent radicals  $-\text{O}-$  or  $-\text{O}(\text{C}(\text{R}_6)_2)_s\text{O}-$ ;

$\text{R}_6$  is hydrogen, alkyl of 1-6 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl of 2-

20 6 carbon atoms, cycloalkyl of 1-6 carbon atoms, carboalkyl of 2-7 carbon atoms, carboxyalkyl (2-7 carbon atoms), phenyl, or phenyl optionally substituted with one or more halogen, alkoxy of 1-6 carbon atoms, trifluoromethyl, amino, alkylamino of 1-3 carbon atoms, dialkylamino of 2-6 carbon atoms, nitro, cyano, azido, halomethyl, alkoxymethyl of 2-7 carbon atoms, alkanoyloxymethyl of 2-7 carbon atoms, alkylthio of 1-6 carbon atoms, hydroxy, carboxyl, carboalkoxy of 2-7 carbon atoms, phenoxy, phenyl, 25

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- 149 -

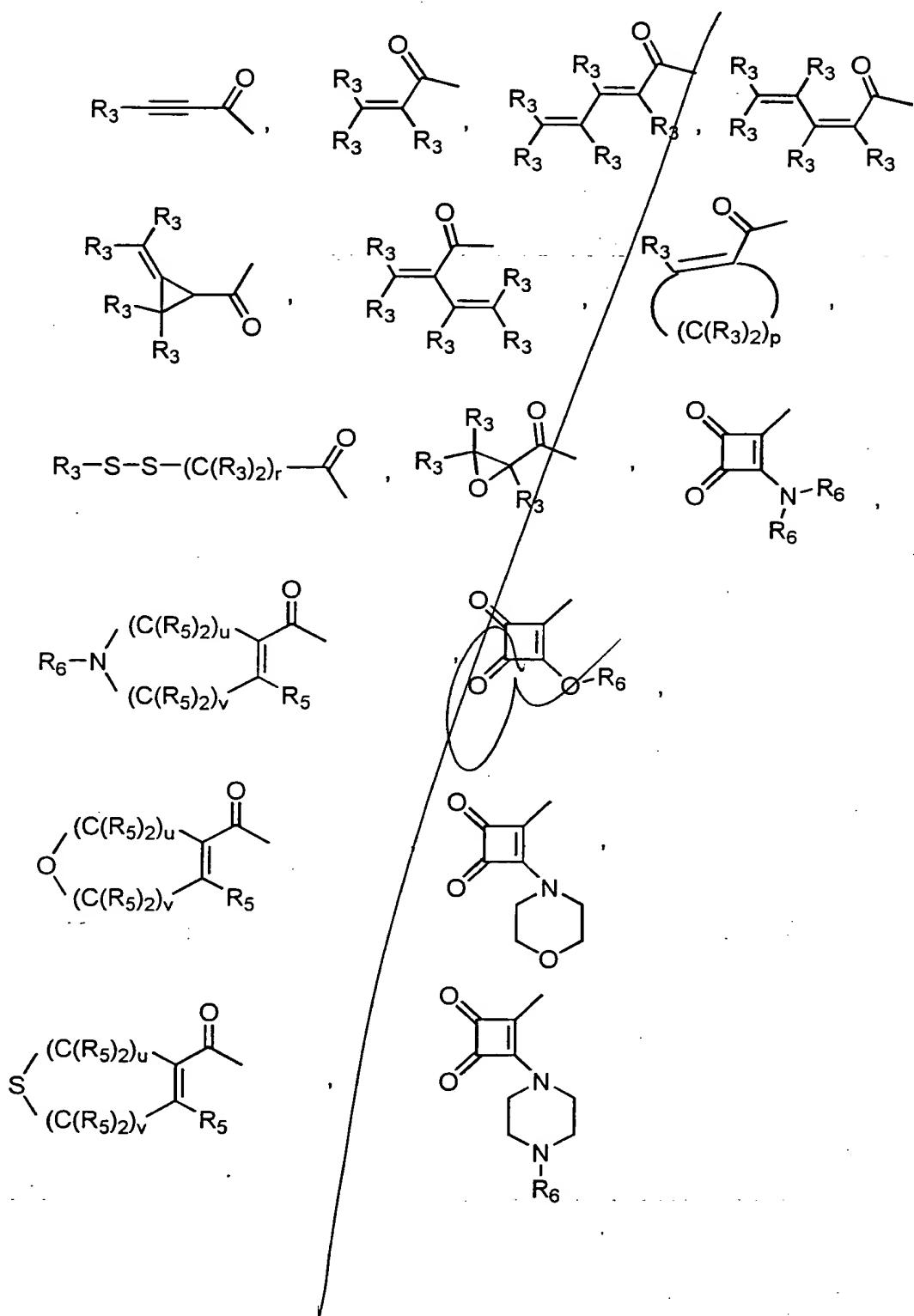
thiophenoxy, benzoyl, benzyl, phenylamino, benzylamino, alkanoylamino of 1-6 carbon atoms, or alkyl of 1-6 carbon atoms;

R<sub>2</sub>, is selected from the group consisting of

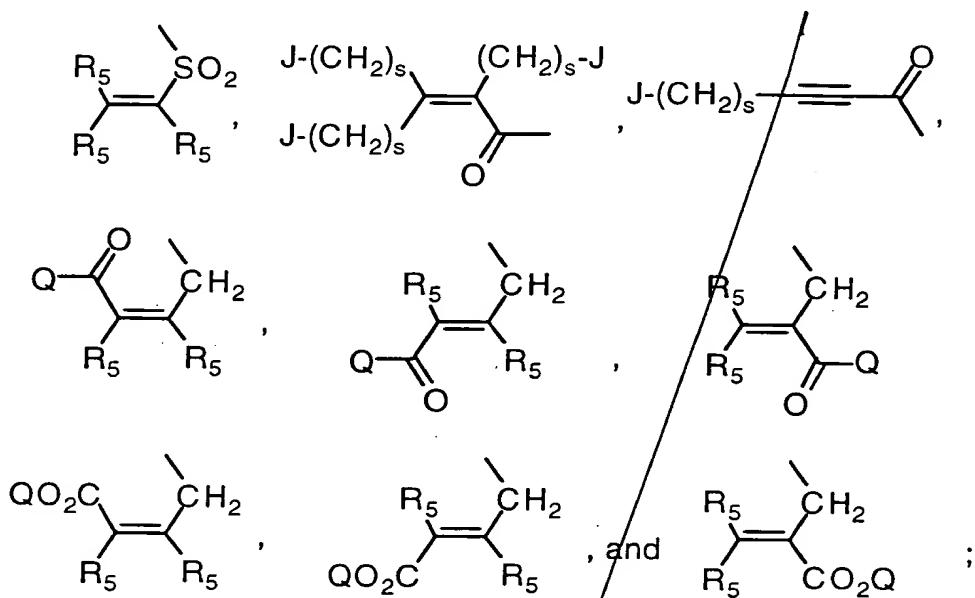
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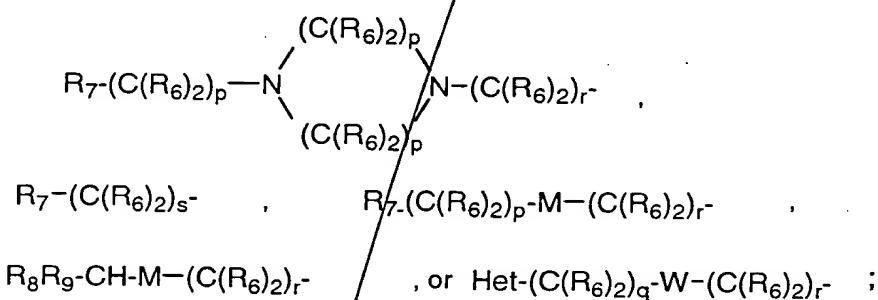
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- 151 -

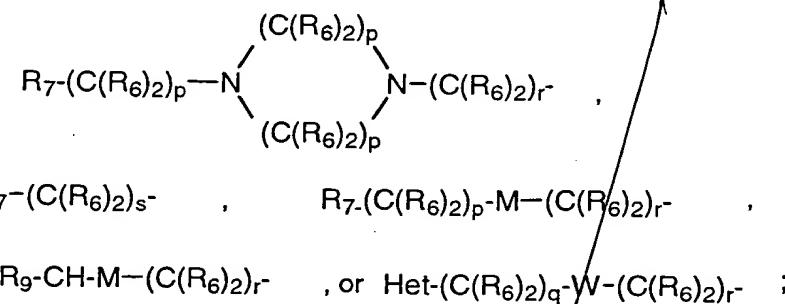


R3 is independently hydrogen, alkyl of 1-6 carbon atoms, carboxy, carboalkoxy of 1-  
5 6 carbon atoms, phenyl, carboalkyl of 2-7 carbon atoms,



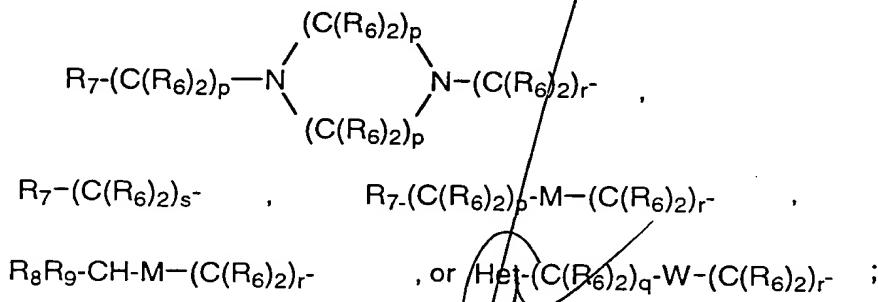
with the proviso that at least one of the R3 groups is selected from the group

- 152 -



R<sub>5</sub> is independently hydrogen, alkyl of 1-6 carbon atoms, carboxy, carboalkoxy of 1-6 carbon atoms, phenyl, carboalkyl of 2-7 carbon atoms,

5



R<sub>8</sub>, and R<sub>9</sub> are each, independently,  $-(\text{C}(\text{R}_6)_2)_r\text{NR}_6\text{R}_6$ , or  $-(\text{C}(\text{R}_6)_2)_r\text{OR}_6$ ;

10

J is independently hydrogen, chlorine, fluorine, or bromine;

Q is alkyl of 1-6 carbon atoms or hydrogen;

a = 0 or 1;

g = 1-6;

15 k = 0-4;

n is 0-1;

p = 2-4;

q=0-4;

r = 1-4;

20 s = 1-6;

u = 0-4 and v = 0-4 , wherein the sum of u+v is 2-4;

- 153 -

or a pharmaceutically acceptable salt thereof,

provided that

when R<sub>6</sub> is alkenyl of 2-7 carbon atoms or alkynyl of 2-7 carbon atoms, such alkenyl or alkynyl moiety is bound to a nitrogen or oxygen atom through a saturated carbon atom;

and further provided that

when Y is -NR<sub>6</sub>- and R<sub>7</sub> is -NR<sub>6</sub>R<sub>6</sub>, -N(R<sub>6</sub>)<sub>3</sub><sup>+</sup>, or -NR<sub>6</sub>(OR<sub>6</sub>), then g = 2-6;

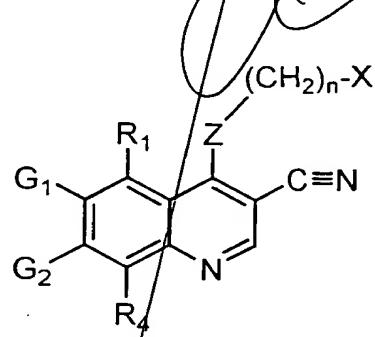
when M is -O- and R<sub>7</sub> is -OR<sub>6</sub>, then p = 1-4;

when Y is -NR<sub>6</sub>-, then k = 2-4;

when Y is -O- and M or W is -O-, then k = 1-4

when W is not a bond with Het bonded through a nitrogen atom, then q = 2-4 and when W is a bond with Het bonded through a nitrogen atom and Y is -O- or -NR<sub>6</sub>-, then k = 2-4.

9. A pharmaceutical composition which comprises a compound of formula 1  
15 having the structure



wherein:

20 X is cycloalkyl of 3 to 7 carbon atoms, which may be optionally substituted with one or more alkyl of 1 to 6 carbon atom groups; or is a pyridinyl, pyrimidinyl, or phenyl ring wherein the pyridinyl, pyrimidinyl, or phenyl ring may be optionally mono-, di-, or tri-substituted with a substituent selected from the group consisting of halogen, alkyl of 1-6 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl of 2-6 carbon atoms, azido, hydroxyalkyl of 1-6 carbon atoms,

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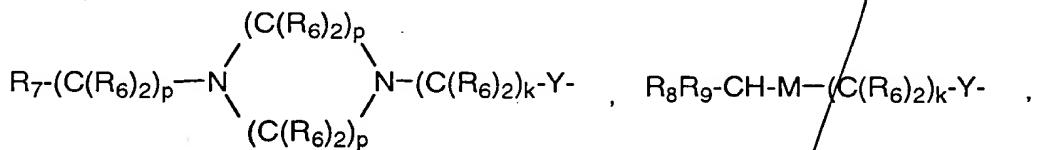
halomethyl, alkoxymethyl of 2-7 carbon atoms, alkanoyloxymethyl of 2-7 carbon atoms, alkoxy of 1-6 carbon atoms, alkylthio of 1-6 carbon atoms, hydroxy, trifluoromethyl, cyano, nitro, carboxy, carboalkoxy of 2-7 carbon atoms, carboalkyl of 2-7 carbon atoms, phenoxy, phenyl, thiophenoxy,  
5 benzoyl, benzyl, amino, alkylamino of 1-6 carbon atoms, dialkylamino of 2 to 12 carbon atoms, phenylamino, benzylamino, alkanoylamino of 1-6 carbon atoms, alkenoylamino of 3-8 carbon atoms, alkynoylamino of 3-8 carbon atoms, carboxyalkyl of 2-7 carbon atoms, carboalkoxyalkyl of 3-8 carbon atoms, aminoalkyl of 1-5 carbon atoms, N-alkylaminoalkyl of 2-9 carbon  
10 atoms, N,N-dialkylaminoalkyl of 3-10 carbon atoms, N-alkylaminoalkoxy of 2-9 carbon atoms, N,N-dialkylaminoalkoxy of 3-10 carbon atoms, mercapto, and benzoylamino;

Z is -NH-, -O-, -S-, or -NR- ;

R is alkyl of 1-6 carbon atoms, or carboalkyl of 2-7 carbon atoms;

15 G<sub>1</sub>, G<sub>2</sub>, R<sub>1</sub>, and R<sub>4</sub> are each, independently, hydrogen, halogen, alkyl of 1-6 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl of 2-6 carbon atoms, alkenyloxy of 2-6 carbon atoms, alkynyoxy of 2-6 carbon atoms, hydroxymethyl, halomethyl, alkanoyloxy of 1-6 carbon atoms, alkenoyloxy of 3-8 carbon atoms, alkynoyloxy of 3-8 carbon atoms, alkanoyloxymethyl of 2-7 carbon atoms, alkenoyloxymethyl of 4-9 carbon atoms, alkynoyloxymethyl of 4-9 carbon atoms, alkoxymethyl of 2-7 carbon atoms, alkoxy of 1-6 carbon atoms, alkylthio of 1-6 carbon atoms, alkylsulphinyl of 1-6 carbon atoms, alkylsulphonyl of 1-6 carbon atoms, alkylsulfonamido of 1-6 carbon atoms, alkenylsulfonamido of 2-6 carbon atoms, alkynylsulfonamido of 2-6 carbon atoms, hydroxy, trifluoromethyl, trifluoromethoxy, cyano, nitro, carboxy, carboalkoxy of 2-7 carbon atoms, carboalkyl of 2-7 carbon atoms, phenoxy, phenyl, thiophenoxy, benzyl, amino, hydroxyamino, alkoxyamino of 1-4 carbon atoms, alkylamino of 1-6 carbon atoms, dialkylamino of 2 to 12 carbon atoms, N-alkylcarbamoyl, N,N-dialkylcarbamoyl, N-alkyl-N-  
20 alkenylamino of 4 to 12 carbon atoms, N,N-dialkenylamino of 6-12 carbon atoms, phenylamino, benzylamino,

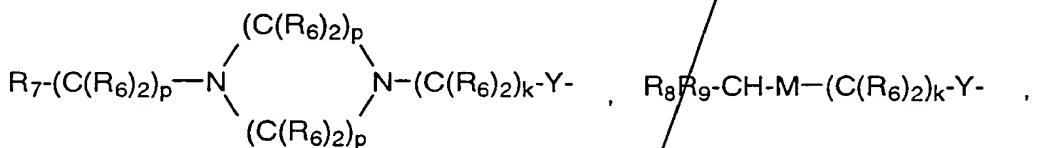
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$R_7-(C(R_6)_2)_g-Y-$ ,  $R_7-(C(R_6)_2)_p-M-(C(R_6)_2)_k-Y-$ , or  $Het-(C(R_6)_2)_q-W-(C(R_6)_2)_k-Y-$

with the proviso that either  $G_1$  or  $G_2$  or both  $G_1$  and  $G_2$  must be a radical selected from the group

5



$R'_7-(C(R_6)_2)_g-Y-$ ,  $R_7-(C(R_6)_2)_p-M-(C(R_6)_2)_k-Y-$ ,  $Het-(C(R_6)_2)_q-W-(C(R_6)_2)_k-Y-$ ,

or  $R_2-N-H$ ;

Y is a divalent radical selected from the group consisting of

10

$-(CH_2)_a-$ ,  $-O-$ , and  $-N-R_6-$ ;

$R_7$  is  $-NR_6R_6$ ,  $-J$ ,  $-OR_6$ ,  $-N(R_6)_3^+$ , or  $-NR_6(OR_6)$ ;

$R'_7$  is  $-NR_6(OR_6)$ ,  $-N(R_6)_3^+$ , alkoxy of 1-6 carbon atoms, alkynoxy of 1-6 carbon atoms,

N-alkyl-N-alkenylamino of 4 to 12 carbon atoms, N,N-dialkenylamino of 6-12 carbon atoms,

N-alkyl-N-alkynylamino of 4 to 12 carbon atoms, N-alkenyl-N-alkynylamino of 4 to 12 carbon atoms, or N,N-dialkynylamino of 6-12 carbon atoms

15 with the proviso that the alkenyl or alkynyl moiety is bound to a nitrogen or oxygen atom through a saturated carbon atom;

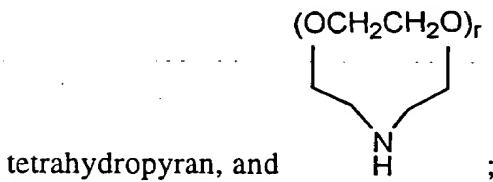
M is  $>NR_6$ ,  $-O-$ ,  $>N-(C(R_6)_2)_pNR_6R_6$ , or  $>N-(C(R_6)_2)_p-OR_6$ ;

20 W is  $>NR_6$ ,  $-O-$  or is a bond

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- 156 -

Het is a heterocycle selected from the group consisting of morpholine, thiomorpholine, thiomorpholine S-oxide, thiomorpholine S,S-dioxide, piperidine, pyrrolidine, aziridine, pyridine, imidazole, 1,2,3-triazole, 1,2,4-triazole, thiazole, thiazolidine, tetrazole, piperazine, furan, thiophene, 5 tetrahydrothiophene, tetrahydrofuran, dioxane, 1,3-dioxolane ,

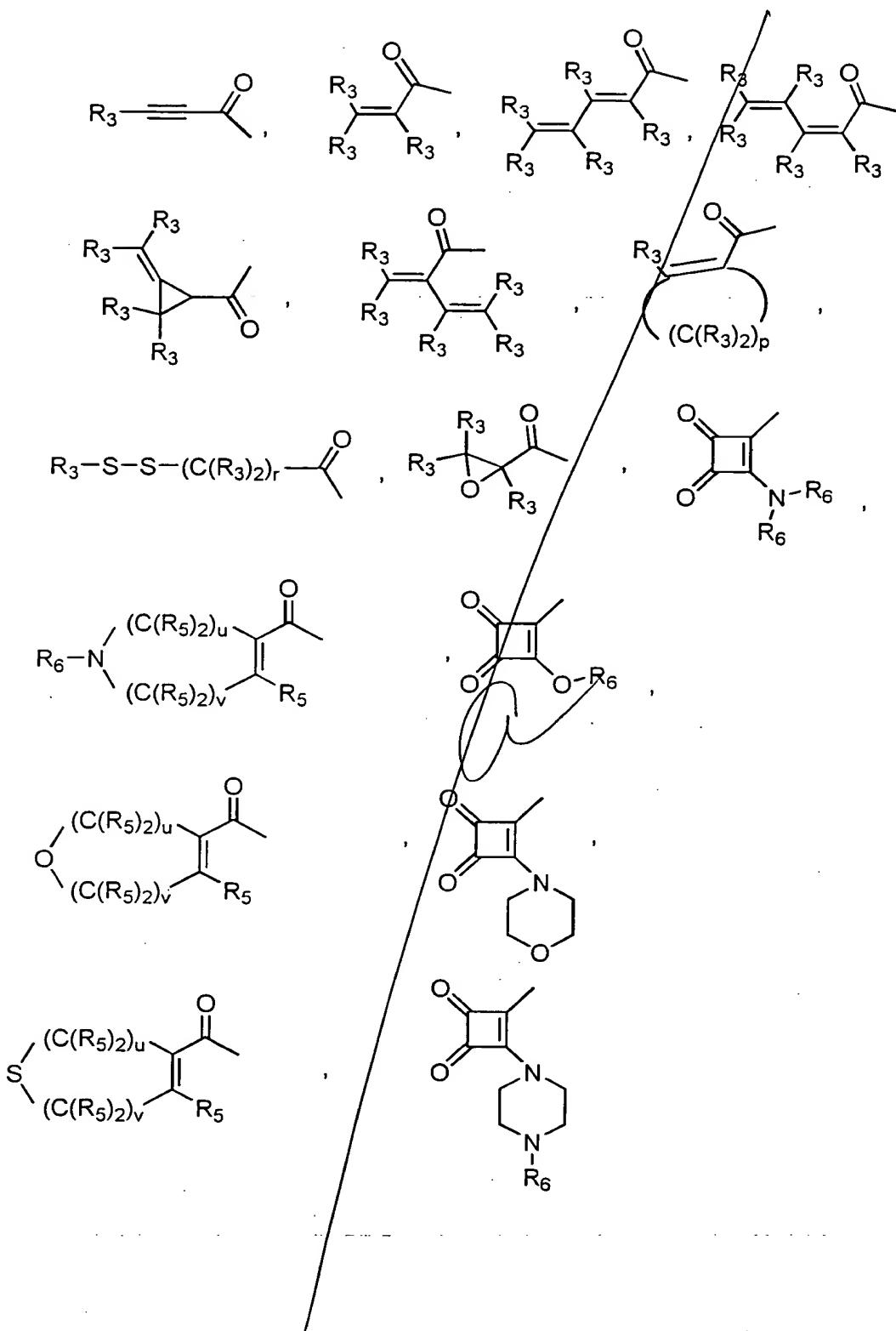


tetrahydropyran, and ;

wherein the heterocycle is optionally mono- or di-substituted on carbon or nitrogen with R<sub>6</sub>, optionally mono- or di-substituted on carbon with hydroxy, -N(R<sub>6</sub>)<sub>2</sub>, or -OR<sub>6</sub>, optionally mono or di-substituted on carbon with the mono-valent radicals -(C(R<sub>6</sub>)<sub>2</sub>)<sub>s</sub>OR<sub>6</sub> or -(C(R<sub>6</sub>)<sub>2</sub>)<sub>s</sub>N(R<sub>6</sub>)<sub>2</sub>, or optionally 10 mono or di-substituted on a saturated carbon with divalent radicals -O- or -O(C(R<sub>6</sub>)<sub>2</sub>)<sub>s</sub>O-;

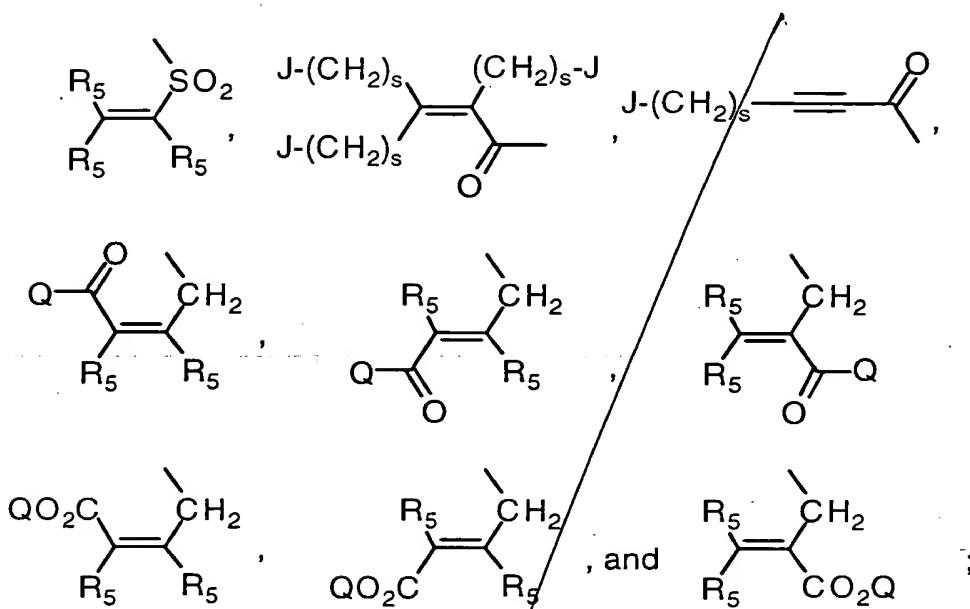
R<sub>6</sub> is hydrogen, alkyl of 1-6 carbon atoms, alkenyl of 2-6 carbon atoms, alkynyl of 2-15 6 carbon atoms, cycloalkyl of 1-6 carbon atoms, carboalkyl of 2-7 carbon atoms, carboxyalkyl (2-7 carbon atoms), phenyl, or phenyl optionally substituted with one or more halogen, alkoxy of 1-6 carbon atoms, trifluoromethyl, amino, alkylamino of 1-3 carbon atoms, dialkylamino of 2-6 carbon atoms, nitro, cyano, azido, halomethyl, alkoxymethyl of 2-7 carbon atoms, alkanoyloxymethyl of 2-7 carbon atoms, alkylthio of 1-6 carbon atoms, hydroxy, carboxyl, carboalkoxy of 2-7 carbon atoms, phenoxy, phenyl, thiophenoxy, benzoyl, benzyl, phenylamino, benzylamino, alkanoylamino of 20 1-6 carbon atoms, or alkyl of 1-6 carbon atoms;

25 R<sub>2</sub>, is selected from the group consisting of

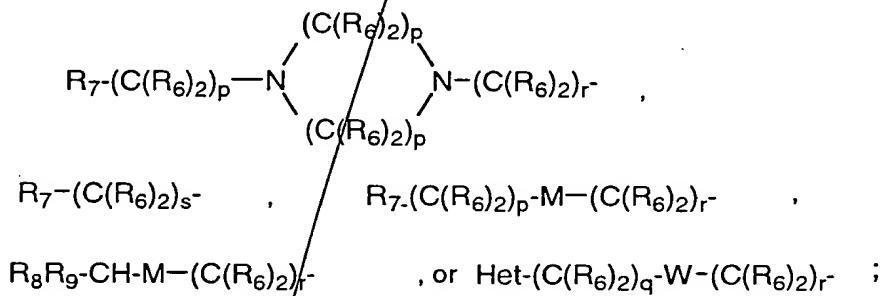


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- 158 -

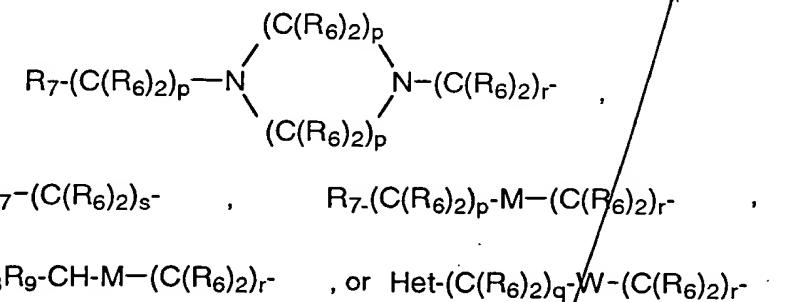


R<sub>3</sub> is independently hydrogen, alkyl of 1-6 carbon atoms, carboxy, carboalkoxy of 1-  
5 6 carbon atoms, phenyl, carboalkyl of 2-7 carbon atoms,



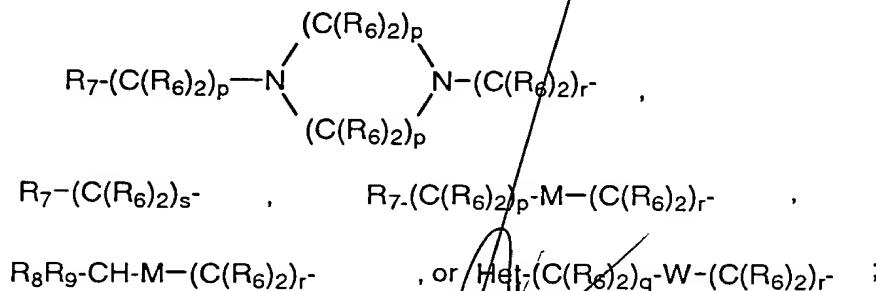
with the proviso that at least one of the R<sub>3</sub> groups is selected from the group

- 159 -



R<sub>5</sub> is independently hydrogen, alkyl of 1-6 carbon atoms, carboxy, carboalkoxy of 1-6 carbon atoms, phenyl, carboalkyl of 2-7 carbon atoms,

5



R<sub>8</sub>, and R<sub>9</sub> are each, independently, -(C(R<sub>6</sub>)<sub>2</sub>)<sub>r</sub>NR<sub>6</sub>R<sub>6</sub>, or -(C(R<sub>6</sub>)<sub>2</sub>)<sub>r</sub>OR<sub>6</sub>;

10

J is independently hydrogen, chlorine, fluorine, or bromine;

Q is alkyl of 1-6 carbon atoms or hydrogen;

a = 0 or 1;

g = 1-6;

15 k = 0-4;

n is 0-1;

p = 2-4;

q=0-4;

r = 1-4;

20 s = 1-6;

u = 0-4 and v = 0-4 , wherein the sum of u+v is 2-4;

- 160 -

or a pharmaceutically acceptable salt thereof,  
provided that

when R<sub>6</sub> is alkenyl of 2-7 carbon atoms or alkynyl of 2-7 carbon atoms, such  
alkenyl or alkynyl moiety is bound to a nitrogen or oxygen atom  
5 through a saturated carbon atom;

and further provided that

when Y is -NR<sub>6</sub>- and R<sub>7</sub> is -NR<sub>6</sub>R<sub>6</sub>, -N(R<sub>6</sub>)<sub>3</sub><sup>+</sup>, or -NR<sub>6</sub>(OR<sub>6</sub>), then g = 2-6;

when M is -O- and R<sub>7</sub> is -OR<sub>6</sub>, then p = 1-4;

when Y is -NR<sub>6</sub>-, then k = 2-4,

10 when Y is -O- and M or W is -O-, then k = 1-4

when W is not a bond with Het bonded through a nitrogen atom, then q = 2-4  
and when W is a bond with Het bonded through a nitrogen atom and Y is -O- or -  
NR<sub>6</sub>-, then k = 2-4.

00000000000000000000000000000000